DOI: 10.1111/apt.16395

INVITED EDITORIAL

AP&T Alimentary Pharmacology & Therapeutics WILEY

# Editorial: on the road towards treatment of gastroparesis—accelerating, but do we get closer? Authors' reply

We thank Dr Wuestenberghs and Professor Gourcerol for their thoughtful response to our manuscript.[1,2] As they note, it is a paradox of gastroparesis treatment that, while the goals are to improve both symptoms and the underlying motility disorder, symptomatic improvement does not correlate well with acceleration of gastric emptying. Our study showed that velusetrag improved gastric emptying. Our lack of data on symptom improvement was mentioned as a limitation of our study in the Discussion section.[2]

We recognise that symptomatic improvement is needed for clinical benefit, and we believe that this could have been shown if the study had been designed with symptom improvement as the primary endpoint and powered accordingly. The velusetrag clinical development programme was designed in accordance with the US Food and Drug Administration (FDA) Guidance for Industry on clinical evaluation of drugs for treatment of gastroparesis.[3] For the phase 2a study reported, the priorities were to establish that velusetrag accelerates gastric emptying in patients with gastroparesis, does not worsen gastric emptying in any subset of patients and does no significant harm in the intended patient population. Once proof of concept and safety in patients with gastroparesis were established, as reported in the manuscript, a phase 2b study of velusetrag in patients with gastroparesis (clinicaltrials.gov NCT02267525) was conducted per FDA guidance for phase 2 efficacy assessment with improvement in gastroparesis symptoms based on patient-reported outcomes (PROs) as the primary endpoint.[3,4] The phase 2b study also piloted the use of a proposed new instrument, a 24-hour version of the Gastroparesis Cardinal Symptoms Index (GCSI-24H), for clinical trials in gastroparesis as suggested by the FDA guidance document.[3] As reported at Digestive Disease Week 2019 and United European Gastroenterology Week 2019, treatment with velusetrag 5 mg vs placebo resulted in numerical improvement in the GCSI-24H total score at week 4 and in all individual symptom domains, particularly in patients with idiopathic gastroparesis.[5,6] This work is in final preparation for manuscript submission, and we anticipate it will be available soon.

Chris N. Barnes, David Shaywitz and Daniel Canafax were employees of Theravance Biopharma US, Inc., at the time the work was performed.

AP&T invited editorial columns are restricted to discussing papers that have been published in the journal. An editorial must have a maximum of 500 words, may contain one table or figure, and should have no more than 10 references. It should be submitted electronically to the Editors via http://mc.manuscriptcentral.com/apt.

## ACKNOWLEDGEMENTS

The authors' declarations of personal and financial interests are unchanged from those in the original article.[2]

## LINKED CONTENT

This article is linked to Kuo et al and Wuestenberghs & Gourcerol papers. To view these articles, visit https://doi.org/10.1111/apt.16344 and https://doi.org/10.1111/apt.16375

Braden Kuo[1]
Chris N. Barnes[2]
Deanna D. Nguyen[2]
David Shaywitz[2]
Maria Grimaldi[3]
Cecilia Renzulli[3]
Daniel Canafax[2]
Henry P. Parkman[4]

[1]*Massachusetts General Hospital, Boston, MA, USA*
[2]*Theravance Biopharma US, Inc., South San Francisco, CA, USA*
[3]*Alfasigma S.p.A., Bologna, Italy*
[4]*Temple University School of Medicine, Philadelphia, PA, USA*
*Email: bkuo@mgh.harvard.edu*

## ORCID

*Braden Kuo* https://orcid.org/0000-0002-7228-7317
*Henry P. Parkman* https://orcid.org/0000-0003-4904-4891

## REFERENCES

1. Wuestenberghs F, Gourcerol G. Editorial: on the road toward treatment of gastroparesis – accelerating, but do we get closer? *Aliment Pharmacol Ther.* 2021;54:183–184.
2. Kuo B, Barnes CN, Nguyen DD, et al. Velusetrag accelerates gastric emptying in subjects with gastroparesis: a multicentre, double-blind, randomised, placebo-controlled, phase 2 study. *Aliment Pharmacol Ther.* 2021;53:1090–1097.
3. Center for Drug Evaluation and Research, Food and Drug Administration, U.S. Department of Health and Human Services. Gastroparesis: Clinical evaluation of drugs for treatment. Guidance for industry. Draft guidance. Clinical/Medical. Revision 1. August 2019. https://www.fda.gov/media/129880/download. Accessed April 8, 2021.
4. The Diabetic and Idiopathic Gastroparesis Efficacy, Safety, and Tolerability (DIGEST) Study (DIGEST). https://www.clinicaltrials.gov/ct2/show/NCT02267525. Accessed April 8, 2021.

  

5. Abell T, Kuo B, Esfandyari T, et al. Velusetrag improves gastroparesis both in symptoms and gastric emptying in patients with diabetic or idiopathic gastroparesis in a 12-week global phase 2b study. *Gastroenterology*. 2019;156:S164.
6. Abell T, Kuo B, Esfandyari T, et al. Efficacy of veluestrag treatment in patients with idiopathic gastroparesis: Subgroup analysis of a phase 2b study. *United European Gastroenterol J*. 2019;7:77-78.